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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,440	03/23/2007	Dominique Bourel	096183-0104	2420

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EXAMINER	
JUEDES, AMY E	
ART UNIT	PAPER NUMBER
1644	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)
	10/576,440	BOUREL ET AL.
	Examiner	Art Unit
	AMY JUEDES	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 September 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *1-10,19 and 29-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-18 and 20-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/23/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of group II, drawn to an antibody having a fixing site for a metallic cation, claims 11-18 and 20-28, in the reply filed on 9/17/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-10, 19, and 29-40 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 11-18 and 20-28 read on the elected invention and are being acted upon.

2. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code on pg. 4. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP §608.01.

3. Claim 22 is objected to for the following informalities: The claim recites that "said antibodies human IgGs" instead of said "antibodies are human IgGs". Correction is required.

4. Claim 14 is rejected under 112 fourth paragraph as being an improper dependent claim since omits an element from the claim upon which it depends. Claim 14 depends from claim 11, which requires an IgG3 antibody comprising the HIS 310 and His 435 residues. Claim 14 recites that at least one of said His residues is replaced by another amino acid (i.e. the antibody of claim 14 does not comprise the His 310 and His 435 residues, as required by claim 11).

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11-18, 21, and 24-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 11-18, 21, and 25-27 are indefinite in the recitation of particular amino acid residues (i.e. His 310 and His 435) of IgG3. The recitation of a particular amino acid residue in the absence of a SEQ ID NO. is indefinite, since residue 310 and 435 might not be the same in all IgG sequences (for example in engineered IgGs, mouse IgG, human IgG, etc).

Regarding claims 24-25 and 28, the phrase "in particular" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient guidance to make an antibody having a fixing site for a metallic cation comprising His 310 and His435, wherein at least one of said His residues is replaced by another amino acid.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation

needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

The instant claim is drawn to an antibody that can fix a metallic cation at the site comprising His 310 and His435, wherein at lease on of the His residues is replaced by another amino acid. The state of the art is such that protein chemistry is one of the most unpredictable areas of biotechnology. Whisstock et al (Quarterly Review of Biophysics, 2003, 36, pp307-340) teach that the prediction of protein function from sequence and structure is a difficult problem, because homologous proteins often have different functions. Even single amino acid changes in a proteins amino acid sequence can have dramatic effects on protein function. For example, Wang et al. , 2001, show that a single amino acid determines lysophospholipid specificity of the S1P1 (EDG1) and LPA1 (EDG2) phospholipids growth factor receptors (e.g., abstract). These references demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein. Thus, given the unpredictability of the art, the instant specification must provide a sufficient and enabling disclosure commensurate in scope with the instant claims. The instant specification discloses that the His 310 and

His435 residues are critical for metallic cation binding. Thus, mutating one of these residues, while still maintaining metallic cation binding at the site would be highly unpredictable, and the instant specification does not provide any examples of antibodies that can function as claimed. Thus, it would require undue experimentation to make and use the antibodies as claimed

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-13 and 15-18 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonagura et al., 1992, as evidenced by Artandi et al., 1991, and Sigma Aldrich.

Bonagura et al. teach a human IgG3 antibody comprising the His310 residue, and in which the Arg435 residue has been replaced by His 435 by molecular engineering (see page 249, in particular). Said antibody is identical to that of the instant claims, and would inherently have a fixing site for a divalent or trivalent metallic cation. Furthermore, IgG3 inherently comprises the His 433 and Asn 434 residues. Additionally, Bonagura et al. teach the IgG3 amino acid sequence of OMM (see page 246, In particular). As evidenced by Artandi et al., 1991, OMM expressed the G3m(g) and G3m(b) allotypes (see page 604, in particular). Furthermore, Bonagura et al. teach expressing the antibodies according to the method of Artandi et al., 1991. Artandi et al. teach that the antibodies are expressed by culturing cells in IMDM medium comprising serum (see page 603, in particular), and harvesting the supernatant. As evidenced by Sigma-Aldrich, Zinc is an essential supplement in cell culture that is provided in serum. Thus, the antibodies of Bonagura et al. are present in a composition comprising cell culture medium, which inherently comprises zinc. Since the antibodies inherently comprise a zinc binding site, they would inherently comprise zinc fixed to said binding site.

Thus, the reference clearly anticipates the invention.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 20-28 are rejected under 35 U.S.C. 102(b) as being anticipated by Badin et al., 1976.

Badin et al. teach compositions of human IgG, including IgG1 in a zinc sulphate solution. Badin et al. teach adding a small amount of antibody solution (0.05ml) to a 2 ml volume of zinc solution. Badin et al. teach that the IgG concentration in the antibody solution is 10 mg/ml, and the zinc concentration in the zinc solution is 1.3g/1000ml (see page 985, in particular). Therefore, the composition of Badin et al. comprises 2.6 mg of zinc (i.e. 2 ml of a 1.3g/100ml solution), and comprises 0.5 mg of antibody (i.e. the zinc concentration is at least equal to the antibody concentration). Badin et al. teach that zinc solution is dissolved in distilled water, which meets the limitation of a pharmaceutical composition, or a composition adapted for injection. Furthermore, human IgG1 antibodies inherently comprise His310, His433, Asn434, and His435 residues that would bind metallic cations.

Thus, the reference clearly anticipates the invention.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes whose telephone number is 571-272-4471. The examiner can normally be reached on 8am to 4:30pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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